REMARKS

This Amendment is filed in response to the Office Action mailed 28 March 2005. A Petition to Extend Time under 37 C.F.R. § 1.136(a) for two (2) months, up to and including Monday, 29 August 2005, is enclosed.

Claims 20-34 and 39-42 remain pending in this application. In response to a previous Restriction Requirement, claims 1-19 and 35-38 were cancelled. Applicants reserve the right to pursue this and any additional subject matter supported within this specification in one or more continuing applications.

Rejection of Claims 20-34 and 39-42 Under §§ 101 and 112, First Paragraph

Pending claims 20-34 and 39-42 stand rejected under both §101 and §102, first paragraph, allegedly "because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility" (§101) and "since the claimed invention is not supported by either a substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention" (§112, first paragraph), respectively. Applicants respectfully disagree. Applicant does assert, at least as of the 10 December 1998 filing date, a "specific and substantial asserted utility." This utility is clearly asserted for the presently claimed invention at least from page 3, line 30 through page 4, line 32. This section of the specification is as follows:

> Northern analysis on the following human tissue samples -- heart, brain, placenta, lung, liver,skeletal muscle, kidney, pancreas, adrenal medulla, thyroid, adrenal cortex, testis, thymus, small intestine and stomach -- reveals that nNR7 and/or nNR7-1 is expressed mainly in liver at medium to low level and the small intestine. It may be expressed at much higher level in other tissues not examined. This data suggest that nNR7 and/or nNR7-1 plays important roles in carrying out metabolic functions involving D vitamins, since the liver is the major site for generation of hydroxylated D vitamins, which are active forms of vitamin D for the vitamin D receptor. It is also possible that other vitamin D metabolites may be active forms for nNR7 and/or nNR7-1 in the liver.
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> As noted above, nNR7 and/or nNR7-1 and are expressed in the liver and small intestine. In humans, the cytochrome P-450 monooxygenase 3A4 (CYP3A4) is mainly expressed in the liver and small intestine. The CYP3A4 protein plays an important role in the biotransformation of drugs, including more than 60% of all clinically used drugs, and its expression

level is markedly induced by those compounds. Therefore, assays that measure the effects of compounds on *CYP3A4* gene expression can predict whether drugs will interact in humans. Because the molecular mechanism underlying this induction is unclear, *CYP3A4* gene induction assays have been almost exclusively dependent upon the use of human liver tissue and primary hepatocytes to date. The nNR7 and/or nNR7-1 nuclear receptor disclosed in this application has been disclosed by Lehmann et al. (1998, *J. Clin. Invest* 102: 1016-1023) subsequent to the priority filing date of this specification. The authors identified a response element located in the *CYP3A4* promoter [5'-TGAACT caaagg AGGTCA-3' (SEQ ID NO:24)] that was shown to bind nNR7 (refered to as hPXR by the authors, but lacking in amino acid 1-32 of nNR7 [SEQ ID NO:2]). The authors suggest that drugs which induce *CYP3A4* gene expression activate nNR7 and initiate transcription through *CYP3A4* promoter. *One of the uses of the DNA molecules and concomitantly expressed proteins of the present invention, including but not limited to nNR7 and nNR7-1, will be useful in assays to identify modulators of CPP3A4 levels in vivo. Therefore, transactivation assays using nNR7 and/or nNR7-1 and theCYP3A4 promoter linked to a reporter gene (such as SEAP -- secreted placental alkaline phosphatase) is one approach for identifying modulators of CYP3A4 levels in vivo.* (emphasis added).

The teaching of the Lehmann reference has been described in detail by Applicant in the previous Amendment, entered 04 March 2002. Therefore, Applicants respectfully take the position that at least as of the 10 December 1998 non-provisional filing date, a specific, asserted utility is disclosed for the nNR7-1 nucleic acids, vectors, transfected hosts and methods associated with this subject matter. In view of the discussion *supra*, Applicant respectfully takes the position that the §§ 101 and §112, first paragraph rejection is overcome. Withdrawal of this rejection is proper and is respectfully requested. To this end, claims 20-34 and 39-42 are in proper form for allowance. Early action to that end is earnestly solicited.

The Examiner is invited to contact the undersigned attorney if clarification is required on any aspect of this response, or if any of the claims are considered to require further amendment to be placed in condition for allowance after entry of this Amendment.

Respectfully submitted,

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